Campylobacter: the actual status and control options

Prof. Jaap A. Wagenaar, DVM, PhD

Dept. Infectious Diseases and Immunology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, the Netherlands

Central Veterinary Institute, Lelystad, The Netherlands

j.wagenaar@uu.nl

Outline

- Campylobacter: facts and fiction
- Case study: milk outbreak
- Attribution: why and how?
- Typing of Campylobacter
- Control options
- Conclusions

Campylobacter

- Gram negative bacterium
- Sensitive for heat, dryness, disinfection,...
  - *C. jejuni* (92% of gastro-intestinal infections)
  - *C. coli* (5% of gastro-intestinal infections)
  - *C. lari*
  - *C. upsaliensis*
  - *C. fetus* (blood cultures - systemic)

Attention!!!

If you have Campylobacter fetus strains (cattle, sheep) in your lab or are doing research projects on C. fetus, please contact me:

j.wagenaar@uu.nl

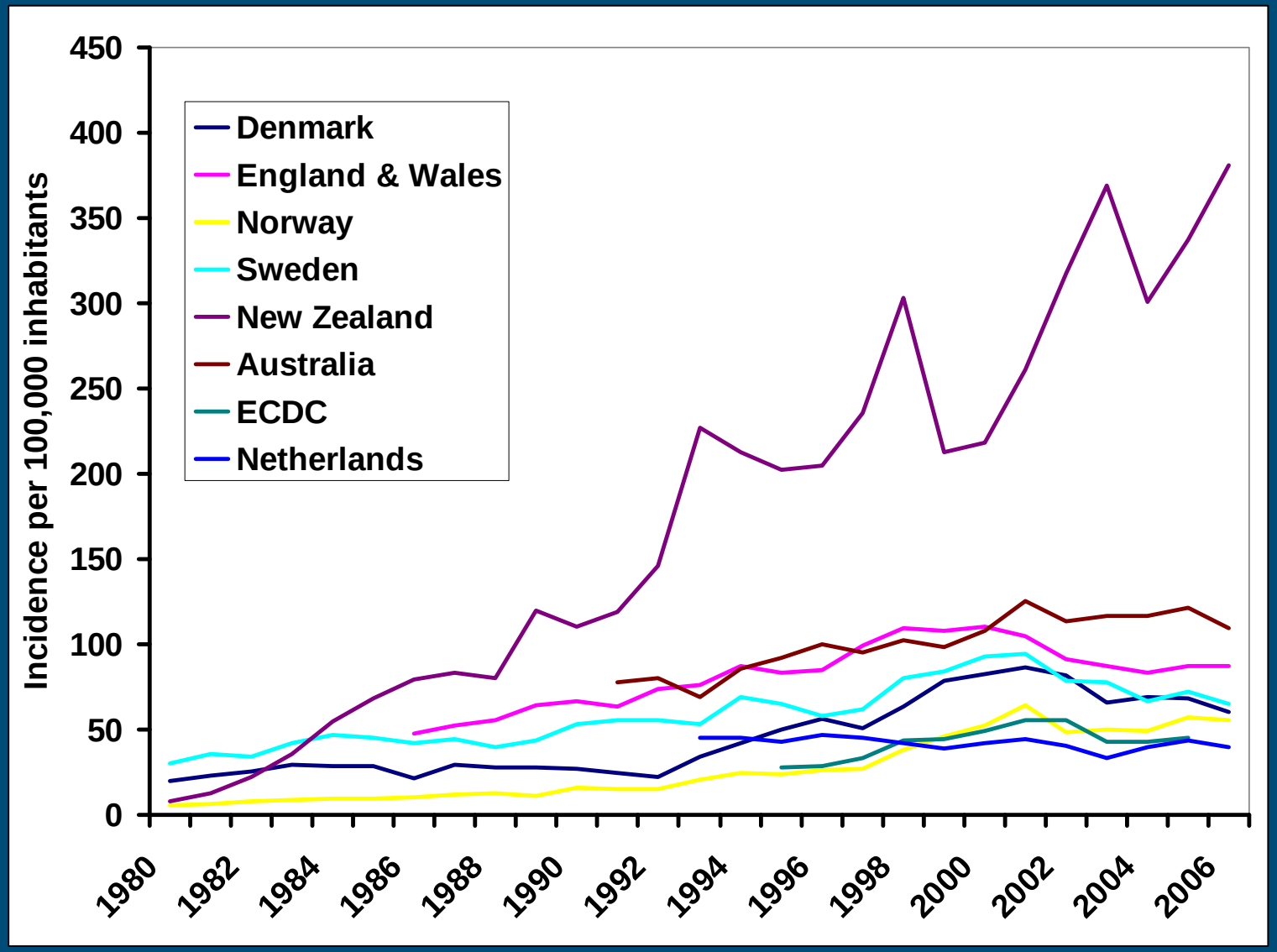
Animal diseases and *Campylobacter*

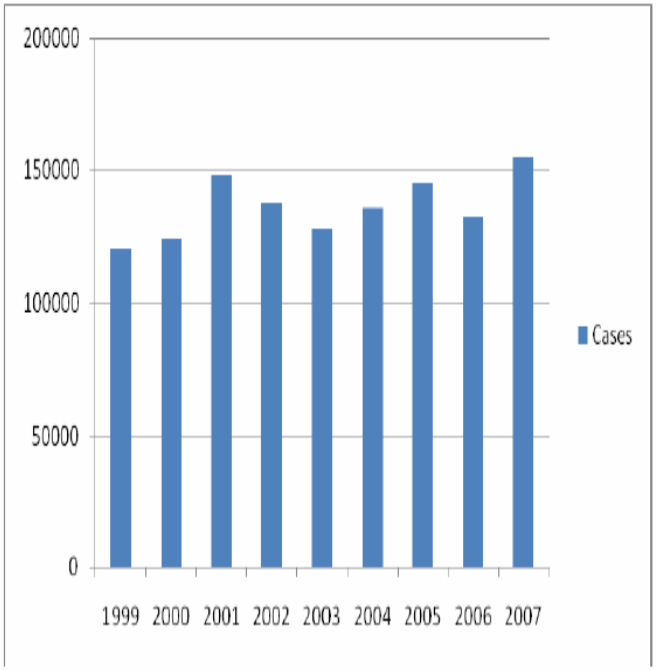
- Many animal species are asymptomatic carrier of *Campylobacter*

- Clinical disease:
  - *C. jejuni* (abortion in cattle and sheep)
  - *C. fetus* subspecies *venerealis*
  - *C. fetus* subspecies *fetus*

Campylobacter and human disease (1)

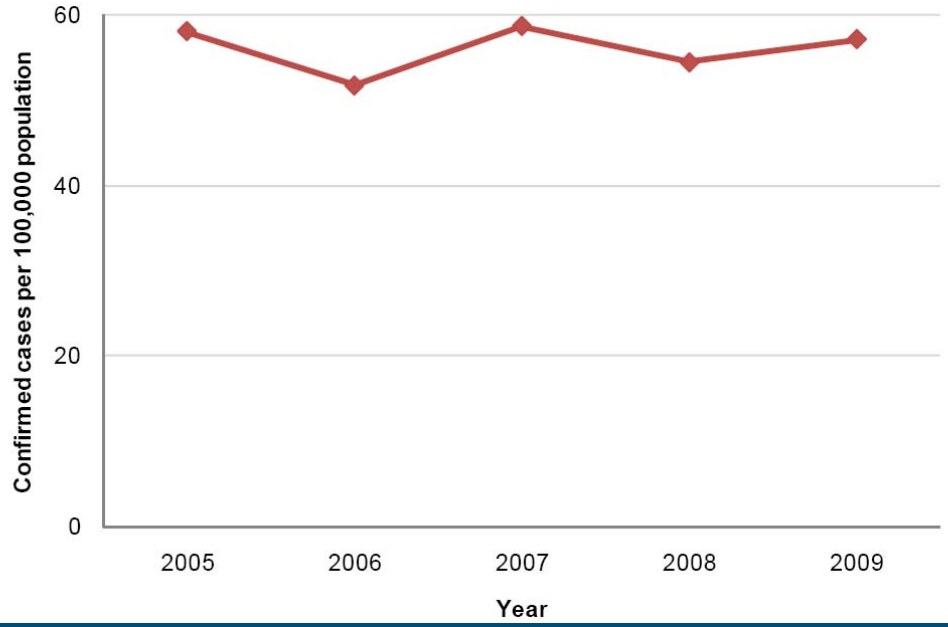
- WHO: 1% of the population per year in the developed world
- Exponential increase end 20th century
- Very strong seasonality (summer peaks)
- Difference in epidemiology in industrialized and developing countries

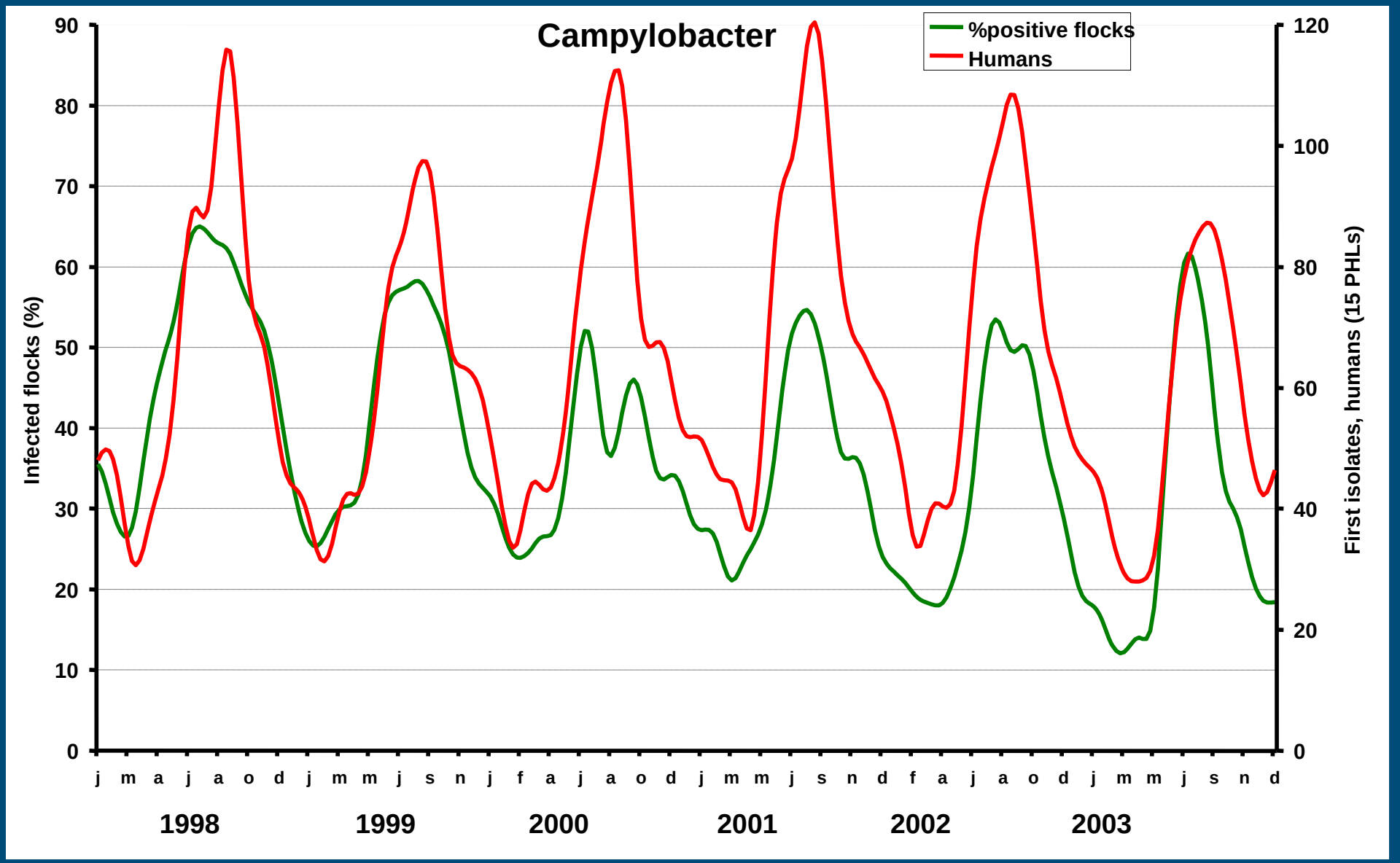

Incidence per 100,000 inhabitants
450
400
350
300
250
200
150
100
50
0
1980
1982
1984
1986
1988
1990
1992
1994
1996
1998
2000
2002
2004
2006
Denmark
England & Wales
Norway
Sweden
New Zealand
Australia
ECDC
Netherlands



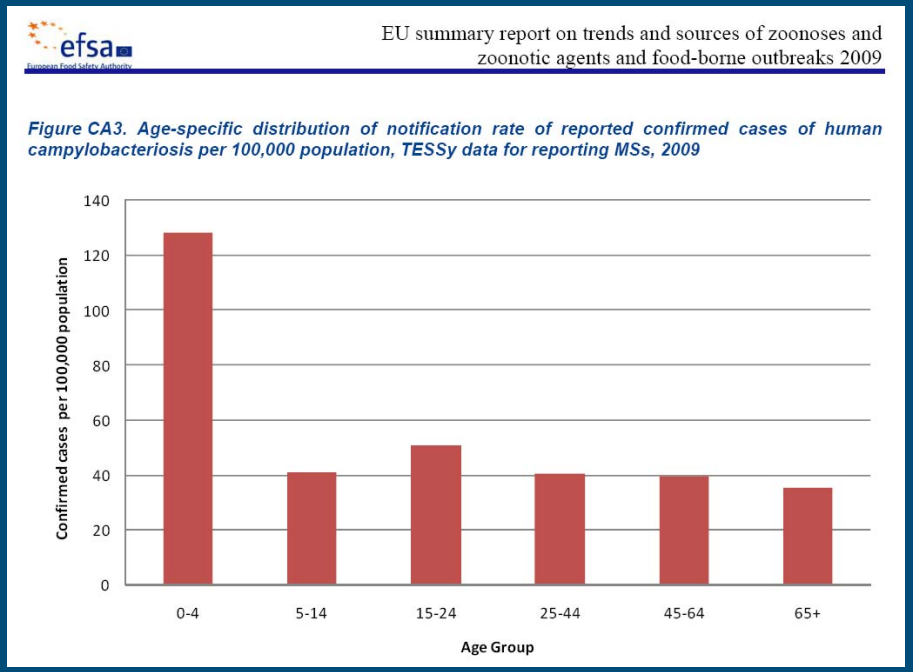
: Campylobacteriosis cases in nine EU MS consistently reporting in the period

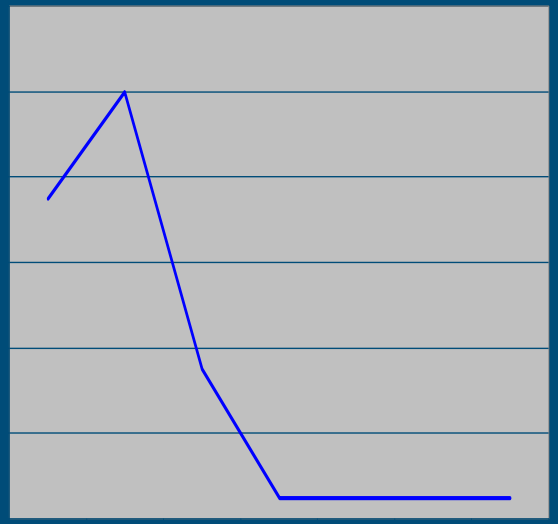
Figure CA1. Notification rates of reported confirmed cases of human campylobacteriosis in EU, 2005-2009




Campylobacter
%positive flocks
Humans
Infected flocks (%)
First isolates, humans (15 PHLs)
0
10
20
30
40
50
60
70
80
90
0
20
40
60
80
100
120
j m a j a o d j m m j s n j f a j a o d j m m j s n d f a j a o d j m m j s n d
1998
1999
2000
2001
2002
2003

Age-specific incidence of *Campylobacter* infections in industrialized and developing nations





Campylobacter and human disease (2)

- Outbreaks are rare or….
- Even a low infectious dose has a considerable risk
- Acute gastro-enteritis (self limiting)
- Sepsis and extra-intestinal infections are rare
- Post-infection complications (1%)
  - Neural and neuromuscular disorders (Guillain Barre Syndrome)

Campylobacter and human disease (3)

- Most common bacterial cause of foodborne disease in Europe; second most common in US
- Common cause of diarrhea in infants and young children in developing countries
- 1999 CDC estimated 2.4 million cases annually in US
  - 13,000 hospitalizations and 120 deaths
- European Union: 10 million cases annually (2009); costs 2.4 billion €
- Global burden ?? (data are lacking)

Cases	Incidence (per 100,000 person years)	Background information
Fatal	0.15-0.30	Extrapolation from Danish registry-based study
Hospitalized	3.5-4.0	Laboratory surveillance
Reported	35-45	Laboratory surveillance
Consulting general practitioner	90-150	GP-based study (NIVEL)
Non-consulting	400-600	Population-based study (Sensor)
Asymptomatic, sero-conversion	10,000-20,000	Sero-surveillance
Asymptomatic, infected	40,000-60,000	Risk assessment model

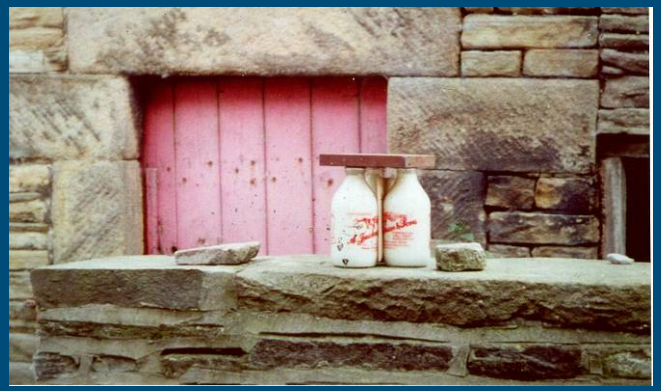
Foodborne Disease Epidemiology Reference Group (FERG):
Initiative to Estimate the Global Burden of Foodborne Diseases.

Top 10 of food borne pathogens (US)

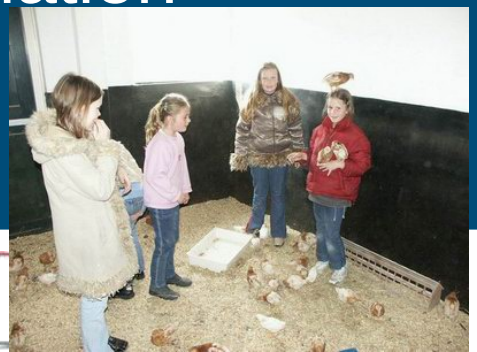
1. Norwalk like viruses	9,200,000
2. Campylobacter	1,963,000
3. Salmonella (non-typhoid)	1,342,000
4. *Clostridium perfringens*	249,000
5. Giardia lamblia	200,000
6. Staphylococcus	185,000
7. Toxoplasma gondii	112,000
8. VTEC (E. coli)	92,000
9. Shigella	90,000
10. Enterotoxigenic E. coli	56,000

Campylobacteriosis: sources of infection

- Poultry meat
- Contaminated drinking water
- Travelling
- Raw milk (case study)
- Direct animal contact



- Cross-contamination



Case study *Campylobacter*

Milk-borne *Campylobacter* outbreak after a school visit on a farm

April 2002…..

- 92 children and 3 teachers visited a farm
- 57 children and 3 teachers drunk fresh milk from the milktank

Met de klas de boer op

Melkveehouderij

Ondernemershandleiding

ALGEMEEN

Ondernemers van Nature

'Met de klas de boer op' is een gezamenlijk project van de Nederlandse boeren en tuinders in het kader van hun campagne 'Ondernemers van Nature'. Zij willen de burgers (en dus ook leerkrachten en leerlingen) meer bij hun werk betrekken en daarom zijn zij in 1998 met deze op dialoog en informatie gerichte campagne gestart. Het logo van de trotse haan en het thema 'Ondernemers van Nature' vormen het 'gezicht' van de campagne, die vanuit de speciaal voor dit doel opgerichte Stichting Hart voor het Land wordt georganiseerd. Voor het project 'Met de klas de boer op' werkt Hart voor het Land samen met het onderwijsprogramma Het Kleine Loo van de Stichting Public Relations Land- en Tuinbouw en met de land- en tuinbouworganisaties NLTO, GLTO, WLTO, ZLTO en LLTB.

De projectmap 'Met de klas de boer op' bestaat uit elf docentenhandleidingen voor lessen over de volgende bedrijfstakken: akkerbouw, volle-grondsgroenteteelt, groenteteelt onder glas, fruitteelt, paddestoelenteelt, teelt van bloemen en planten onder glas, bloembollenteelt, boomkwekerij, melkveehouderij, vleesveehouderij, pluimveehouderij. In de aparte handleiding Agrarisch Nederland wordt een actueel beeld gegeven van de ontwikkelingen in de Nederlandse land- en tuinbouw. Vooral aan de vernieuwingen ten behoeve van duurzaam produceren wordt aandacht besteed.

Bezoek aan het bedrijf en bezoek aan de school

Centraal onderdeel van het project 'Melkveehouderij' voor het basisonderwijs, is het bezoek van een groep aan uw bedrijf of uw bezoek aan de groep op school. De leerkracht van de groep heeft de handleiding ontvangen met achtergrondinformatie over melkveehouderij en de werkzaamheden van de melkveehouder. In deze handleiding staan ook aanwijzingen voor enkele lessen over melkveehouderij en de manier waarop op school het bezoek kan worden voorbereid. Het is ook voor u als ontvangende ondernemer nuttig om deze handleiding in te kijken.

Er zijn dus twee mogelijkheden: een groep brengt een bezoek aan uw bedrijf of u gaat naar de school.
Voor beide mogelijkheden volgen hierna een aantal suggesties die u wellicht kunnen helpen bij het voorbereiden op het bezoek.

■ Laat de leerkracht de kinderen eventueel in kleine groepen verdelen. De kinderen blijven in de groepen bij elkaar en gaan niet op eigen houtje over het bedrijf zwerven.

■ Las halverwege een korte pauze in. De kinderen komen weer bij elkaar en er is gelegenheid om iets te eten en/of te drinken. De kinderen kunnen dan meteen hun eerste indrukken kwijt en vragen stellen. U kunt in de pauze de kinderen verse melk laten proeven. Vraag wat ze ervan vinden

■ Spreek een eindtijd af.

■ Zorg dat de kinderen na afloop hun handen kunnen wassen en naar het toilet kunnen gaan.

■ Geef de kinderen aan het einde van het bezoek iets mee. Denk aan bijvoorbeeld: stro, hooi, voer, melk, een oormerk, oude tijdschriften over de melkveehouderij, kunstmelk, een oude tepelhouder, mest (in een gesloten pot), kunstmest.

Six days after the farm visit…..

- 28 children ill (watery diarrhoea, some with blood and fever >40°C)
- common exposure: farm visit
- questionnaire: milk

Relationship milk/case

	Case:	Yes	No	total
Milk:	Yes	28	29	57
	No	2	33	35
	Total	30	62	92

Dose-respons relation

Case:		yes	no	total	%-case	rel.risk
Milk:	No	2	33	35	6	1.0
	1 swig	2	10	12	17	2.9
	1/2 cup	7	11	18	39	6.8
	1 cup	13	8	21	62	10.8
	2 cups	6	0	6	100	17.5
	total	30	63	92		

Culture of *Campylobacter*

17 days after the visit 18 samples:

- 11 positive direct (all patients)
- 1 positive after enrichment (control)
- 6 negative (all controls)

no sample from the milktank

Discussion

- Farmer was not convinced
- Milk can be contaminated with feces
- Many outbreaks described
- Consumption of raw milk?

Source attribution and the expected impact of control

Human illness source attribution methods

Methodologies for attribution of human illness to specific sources

Approaches	Methods
Microbiological approaches	Microbial subtyping
	Comparative exposure assessment
Epidemiological approaches	Analysis of sporadic cases
	Analysis of data from outbreak investigations
Intervention studies	
Expert elicitation	

Microbiological approaches: microbial subtyping

- Typing: discrimination within a species (vs. speciation)
- Compare with *Salmonella*

Typing *Campylobacter*

- Serotyping (lack of antisera)
  - Heat-stabile (Penner)
  - Heat-labile (Lior)

- Molecular typing
  - Fla (flagellin) typing
  - PFGE (Pulsed Field Gel Electrophoresis)
  - AFLP (Amplified Fragment Length Polymorphism)
  - MLST (Multi Locus Sequence Typing)

Multi Locus Sequencing Typing

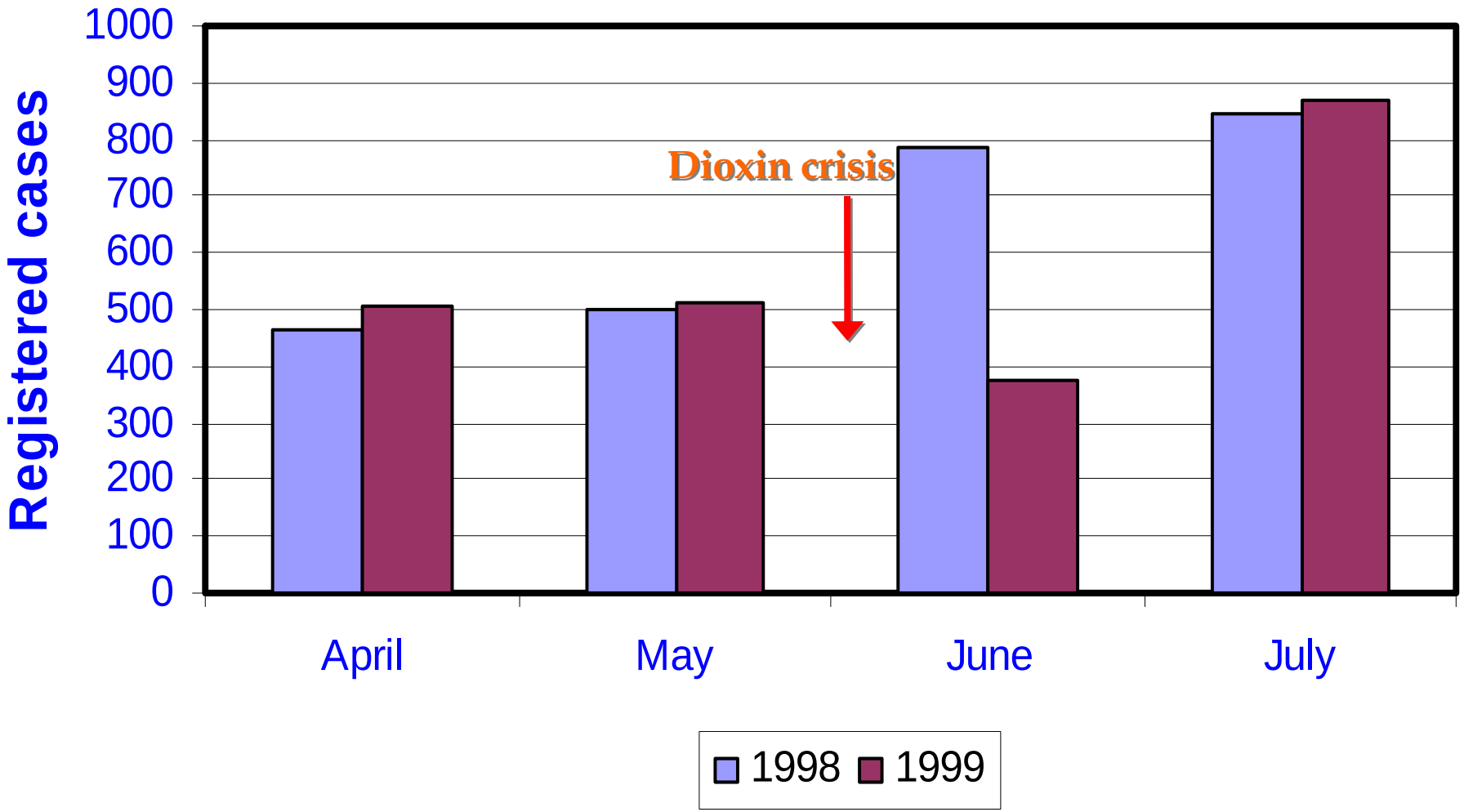
- Sequence of 7 house keeping genes for each strain
- Combination of 7 genes results into Sequence Type (ST)
- Strains from different sources (chicken, cattle, dog, human)
- All information in 1 database (Oxford, UK)
- Mathematical modelling…..
- Outcome: what strains in humans are most likely from…..

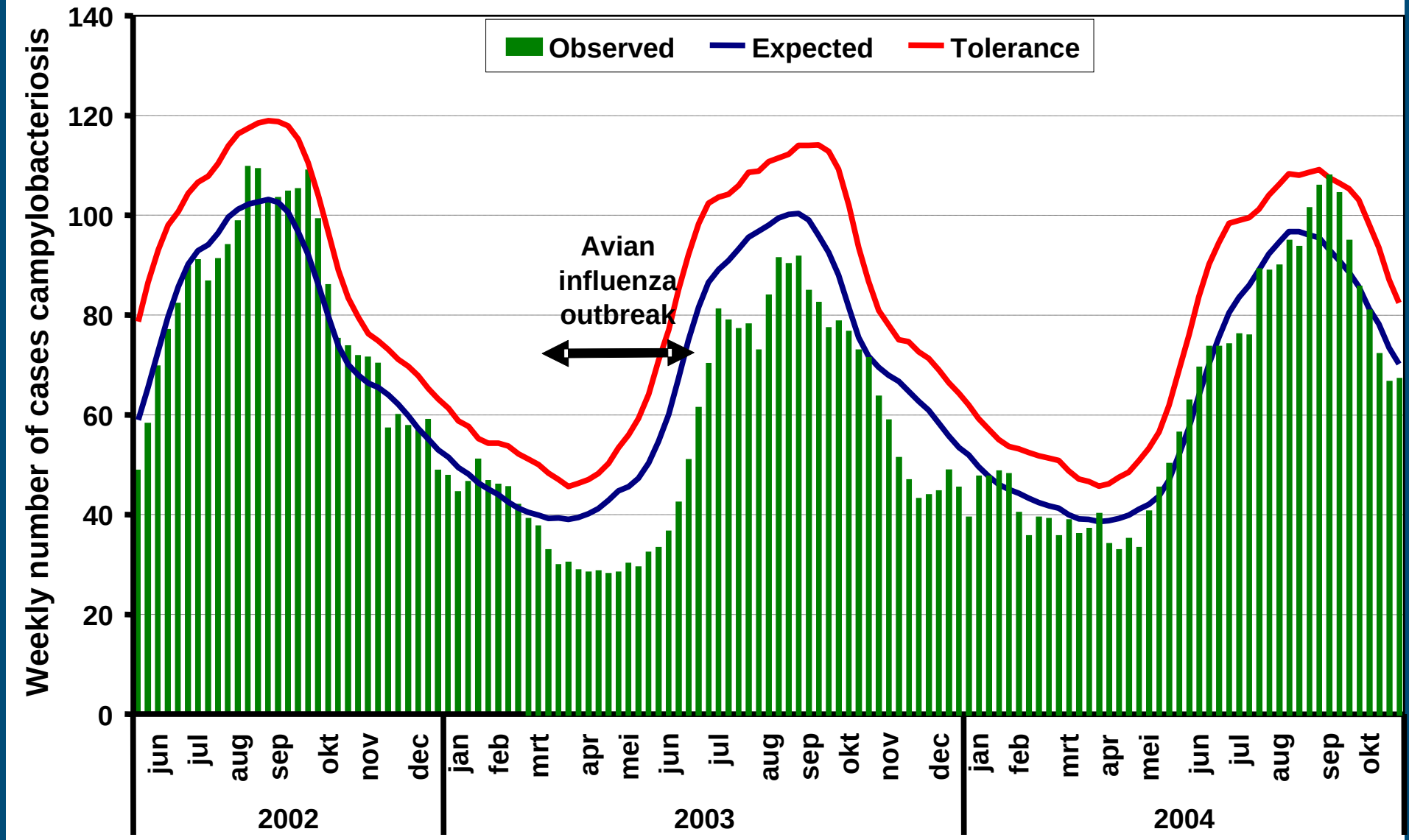
Source attribution: Epidemiological approaches

- Analysis of sporadic cases (e.g. case control studies)
- Investigations of outbreaks

Attribution by analysis of intervention studies

Campylobacteriosis incidence in Belgium




Observed
Expected
Tolerance
Weekly number of cases campylobacteriosis
140
120
100
80
60
40
20
0
Avian influenza outbreak
jun
jul
aug
sep
okt
nov
dec
jan
feb
mrt
apr
mei
jun
jul
aug
sep
okt
nov
dec
jan
feb
mrt
apr
mei
jun
jul
aug
sep
okt
2002
2003
2004

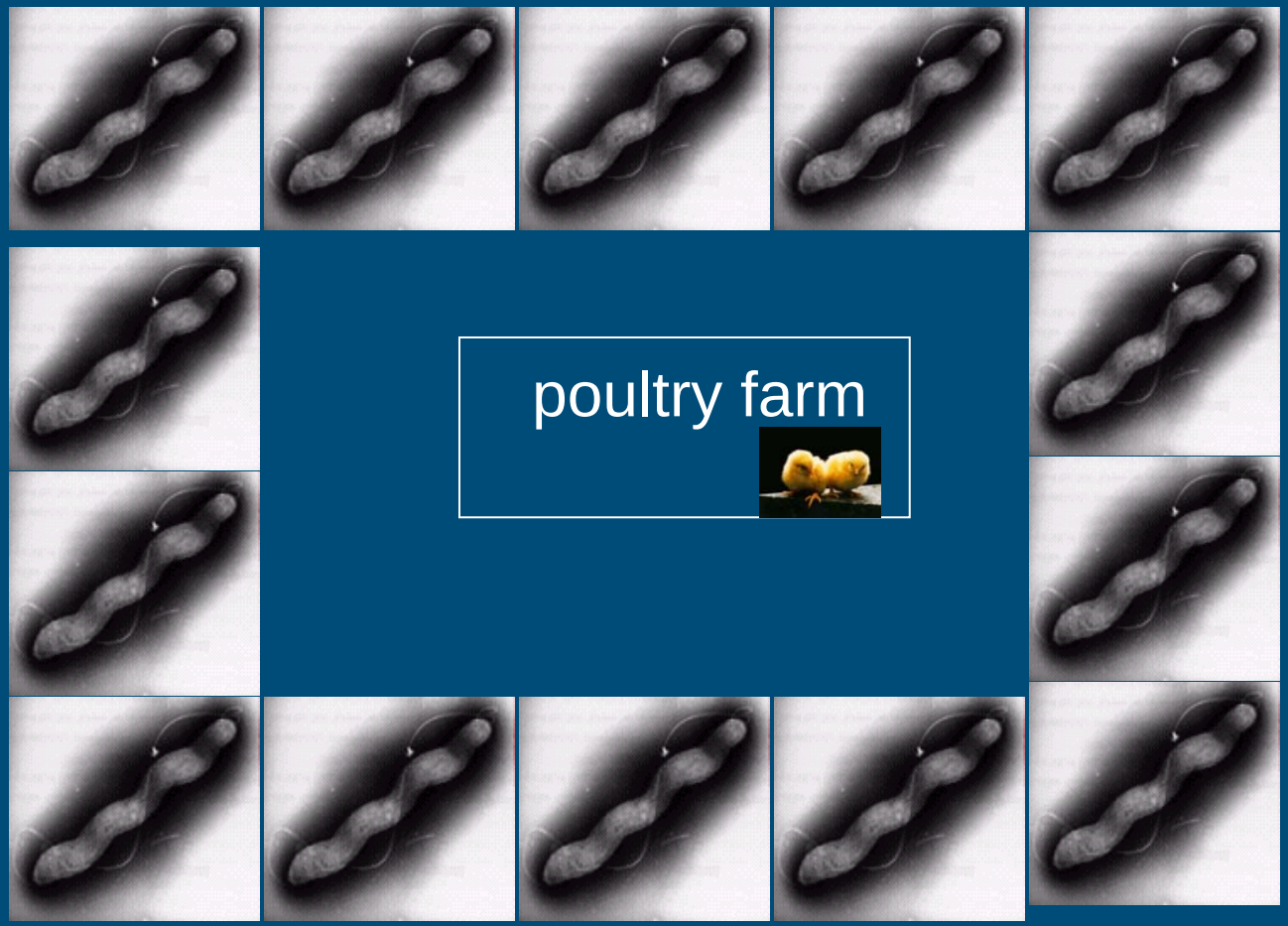
Attribution based on different approaches

- Case control studies: 24-29% attributed to poultry meat
- Outbreaks: 29% attributed to poultry meat

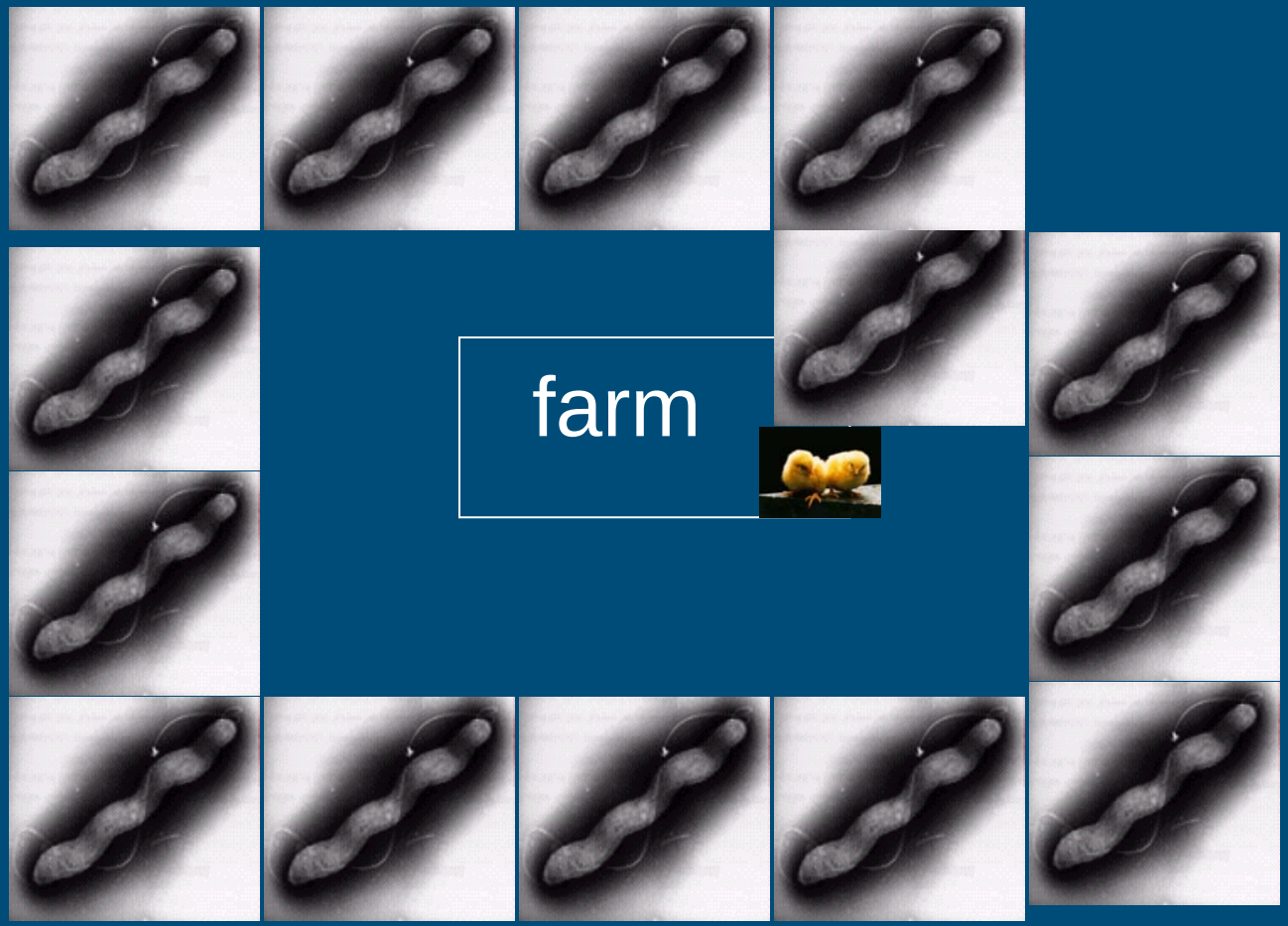
- Microbial subtyping: 50-80% poultry meat!

Interventions in the poultry meat production chain

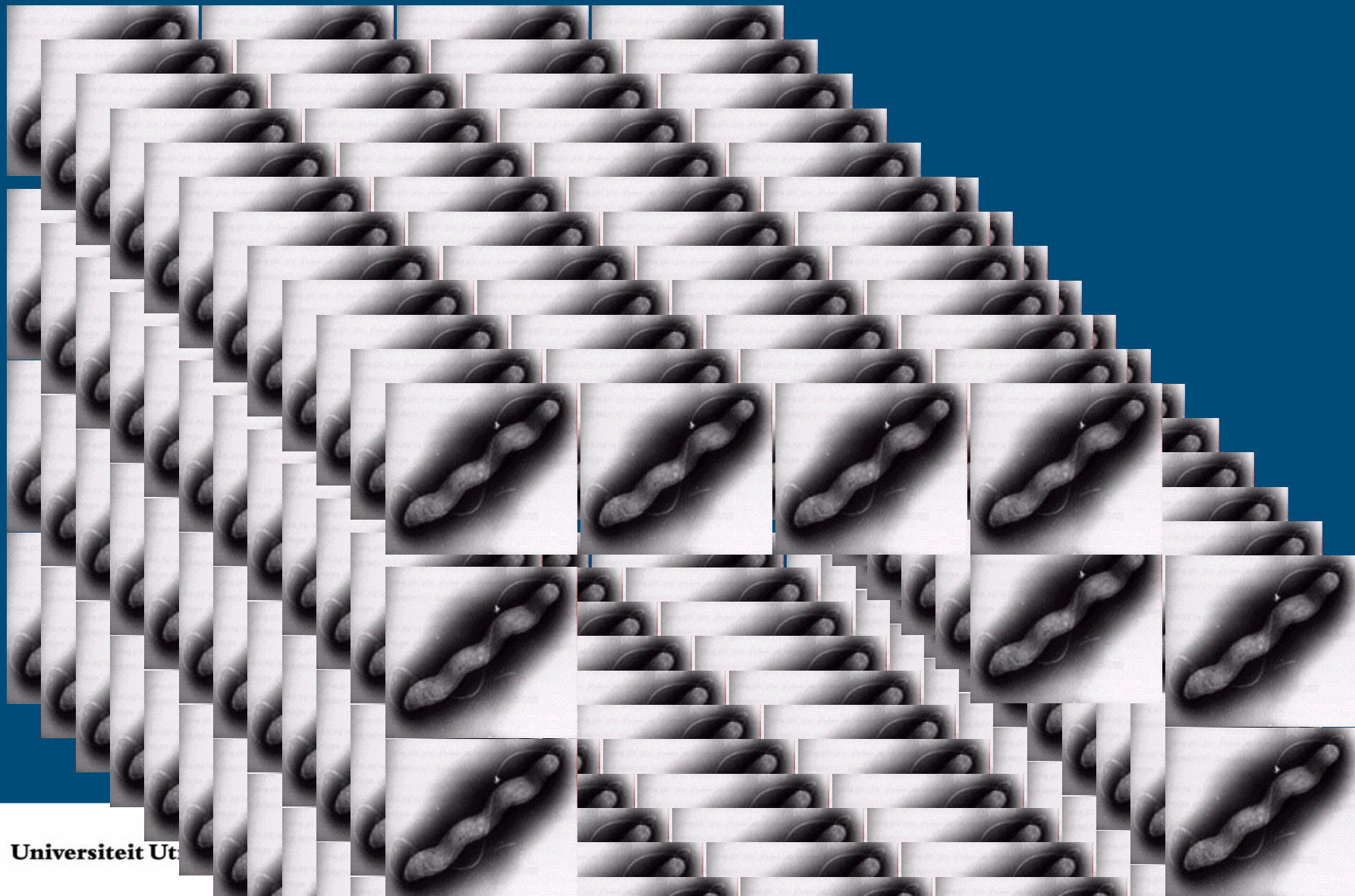
Prevention of introduction of Campylobacter: biosecurity



Prevention of introduction of Campylobacter



Prevention of introduction of Campylobacter



Biosecurity

Campylobacter replicates in chickens

1 broiler can be become colonised with 50 campylobacters

25 gram caecal content x 10^9 x 25,000 broilers =

6.10^{14} campylobacters/day

Cleaning between cycles

6.10^{14} campylobacters (produced daily)

Please don’t forget the last 50 campy’s……

Risk factors for farms to be campy positive (….intervention)

Increased

- Thinning
- Other animals
- Other poultry houses
- Age
- Water

Decreased

- Season
- Implementation of biosecurity measures

Interventions: recent report of EFSA

- If biosecurity is OK, fly screens reduce public health risk by 50-90%
- Stopping thinning: reduces risk by 25%
- Lowering broiler age 35 => 28 days: risk reduction 10-50%
- Scheduled slaughter
- Carcass treatment (acid, chloride, hot water, freezing) reduces risk with 50-90%

Other measures

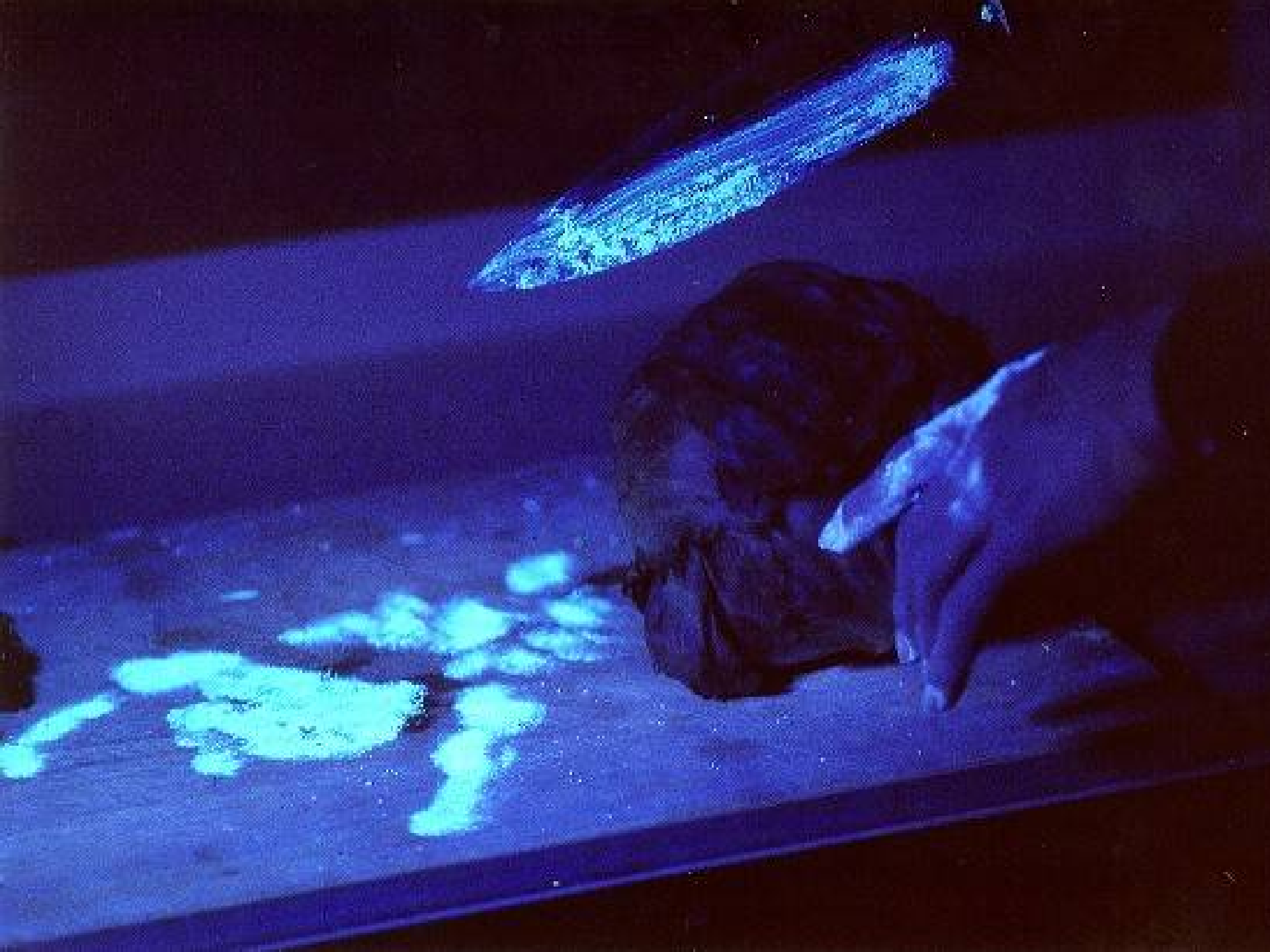
- Vaccination
- Competitive exclusion, probiotics, bacteriocines

Summary

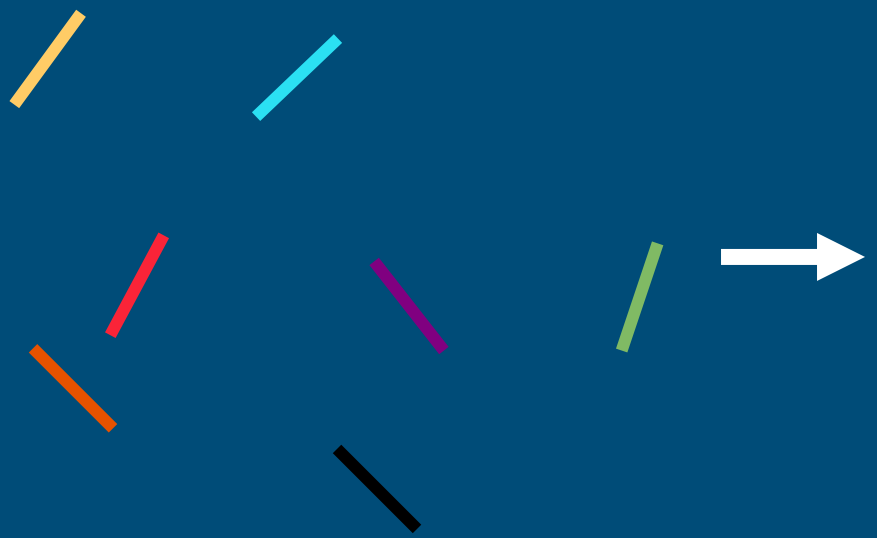
- *Campylobacter* is the leading bacterial cause of enteric illness in the developed and developing world
- Associated with considerable acute and chronic morbidity
- Major risk factor in developed countries: fresh poultry meat, pets, travel abroad, raw milk
- Major risk factor in developing countries: water and animal contact
- Up to 80% is poultry derived with 20-40% poultry meat source
- Options for intervention in primary production are (economically) limited
- From Europe and US tendency to require production of Campy-free poultry meat

Instructions for the consumer!!!

Dr. Henk van der Zee, Food Inspectorate, the Netherlands




Diergeneeskunde



aspA

glnA

gltA

glyA

tkt

MLST analyse (voorbeeld)

Strain	*aspA*	*glnA*	*gltA*	*glyA*	*pgm*	*tkt*	*unc*A	ST
1.	1	1	1	1	1	1	1	1
2.	1	2	2	2	1	2	1	2
3.	1	2	2	3	2	1	1	3
4.	1	1	1	1	1	1	1	1
5.	2	2	2	2	1	2	1	4

Campylobacter MLST Home Page - Microsoft Internet Explorer

Bestand Bewerken Beeld Favorieten Extra Help

Vorige Zoeken Favorieten Geschiedenis

Adres http://pubmlst.org/campylobacter/ Ga naar Koppelingen

msn Search Highlight Options Hotmail Messenger My MSN

Campylobacter MLST Home Page

The Campylobacter MLST database has undergone re-organisation to split allelic profiles from isolate data. The original MLST database has become PubMLST and a new profiles database has been created. Further details about the database structure can be found here.

- Information
- Access main databases
  - Allelic Profile/ST Database
  - PubMLST Isolate Database
- Policy document
- Submission of data
- News and updates

- mlstdbNet software
- Other software
- Related links
- Recent publications using MLST in Campylobacter research

The use of this database is subject to the terms of the policy document and it should be acknowledged in all publications that make use of it. The preferred format for the acknowledgement can be found in the right-hand sidebar.

Website and database managed by Keith Jolley, curated by Kate Dingle.

The primary Campylobacter MLST website is hosted at The Peter Medawar Building for Pathogen Research, University of Oxford, UK. Initial development funded by the Wellcome Trust.

Citing the database

The preferred format for citing this website in publications is:

This publication made use of the Campylobacter Multi Locus Sequence Typing website (http://pubmlst.org/campylobacter/) developed by Keith Jolley and Man-Suen Chan and sited at the University of Oxford (Jolley et al. 2004, *BMC Bioinformatics*, **5**:86). The development of this site has been funded by the Wellcome Trust.

Status

Profile database
Profiles: 1014
Last updated: 2004-09-03

Isolate database
Isolates: 2351
Last updated: 2004-09-03

Internet

Universiteit Utrecht

CENTRAL VETERINARY INSTITUTE WAGENINGEN UR